

IN THE CLAIMS:

Claims 4, 8, 9, 16, 20, 27, 28, 36, 40, 41, and 43-64 were previously cancelled. Claim 2 is canceled herein. Claims 1, 3, 5-7, 10, 11, 13, 14, 17, 19, 21, 22, 25, 26, 29, 31-35, 37-39, 42, and 65-68 have been amended herein. New claims 69 - 72 are to be added. All of the pending claims are presented below. This listing of claims will replace all prior versions and listings of claims in the application. Please enter these claims as amended.

Listing of the Claims:

1. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species, said *thyA* mutant comprising:

an inactive *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule, wherein the inactive *Lactococcus* thymidylate synthase gene has been inactivated by gene disruption;

wherein said parent strain of *Lactococcus* species comprises a thymidylate synthase gene comprising

at least 100 contiguous nucleotides that are at least 90% identical to SEQ ID NO: 1; and

at least 100 contiguous nucleotides that are at least 90% identical to SEQ ID NO: 2, and wherein the *thyA* mutant expresses the heterologous therapeutic molecule.

2. (Canceled).

3. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of any one of claims 1, [[2,]] 5, or 6, wherein the *Lactococcus* species is *Lactococcus lactis*.

4. (Cancelled).

5. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of claim 1, wherein said (*thyA*) mutant is ~~further~~ transformed with a transforming plasmid,

wherein said transforming plasmid does not encode an active thymidylate synthase.

6. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of claim 5, wherein the transforming plasmid comprises the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule.

7. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of any one of claims 1, [[2,]] 5, or 6, wherein the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10.

8-9. (Cancelled).

10. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of any one of claims 1, [[2,]] 5, or 6, wherein gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10 and wherein the *Lactococcus* species is *Lactococcus lactis*.

11. (Withdrawn, currently amended) A method for delivering a heterologous ~~prophylactic or~~ therapeutic molecule to a subject, said method comprising administering the transformed strain of *Lactococcus* species of any of claims 1, 21, 32, and 67 to the subject.

12. (Previously presented) A composition comprising:
the isolated thymidylate synthase (*thyA*) mutant of claim 1.

13. (Currently amended) The composition of claim 65, wherein the transforming plasmid comprises the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule.

14. (Currently amended) The composition of any of claims 12, ~~15~~, 13, or 65, wherein the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10.

15. (Previously presented) The composition of any of claims 12, 13, or 65, wherein said *Lactococcus* species is *Lactococcus lactis*.

16. (Cancelled).

17. (Currently amended) The composition of any of claims 12, 13, or 65, wherein the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10 and wherein said *Lactococcus* species is *Lactococcus lactis*.

18. (Withdrawn) A method of treating inflammatory bowel disease in a subject, said method comprising:

administering to the subject a transformed strain of *Lactococcus* species of any of claims 1, 21, 32, and 67.

19. (Withdrawn and currently amended) The method of claim 18, wherein the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10.

20. (Cancelled).

21. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species, wherein said *thyA* mutant is devoid of thymidylate synthase activity and comprises ~~comprising~~:

lacking an inactive active *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule,

wherein the *thyA* mutant expresses the heterologous therapeutic molecule.

22. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species, said *thyA* mutant comprising:
an inactive *Lactococcus* thymidylate synthase gene; and
a gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule;
wherein said parent strain ~~of *Lactococcus* species~~ comprises ~~a nucleotide sequence~~
~~selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5,~~
wherein the *thyA* mutant expresses the heterologous therapeutic molecule.

23. (Previously presented) The isolated thymidylate synthase (*thyA*) mutant of any of claims 21, 24, or 25, wherein the *Lactococcus* bacterium is a *Lactococcus lactis* bacterium.

24. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 21, further comprising a transforming plasmid; and
wherein said transforming plasmid does not encode an active thymidylate synthase.

25. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of claim 24, wherein the transforming plasmid comprises the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule.

26. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of any of claims 21, 24, or 25, wherein the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10.

27-28. (Cancelled).

29. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of any of claims 21, 24, or 25, wherein the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10 and wherein the *Lactococcus* species is *Lactococcus lactis*.

30. (Previously Presented) A composition comprising: the isolated thymidylate synthase (*thyA*) mutant of claim 21.

31. (Currently amended) The isolated *thyA* mutant of a parent strain of *Lactococcus* species of claim 1, wherein said parent strain ~~of *Lactococcus* species comprises an active *Lactococcus* thymidylate synthase comprising a nucleotide sequence selected from the group consisting of~~ comprises SEQ ID NO: 3 ~~[[and]]~~ or SEQ ID NO: 5.

32. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species, wherein said *thyA* mutant ~~comprises an inactive~~ lacks active *Lactococcus* thymidylate synthase gene and comprises a gene encoding a heterologous ~~prophylactic or therapeutic molecule, wherein the *thyA* mutant expresses the heterologous therapeutic molecule,~~ and wherein said *thyA* mutant is produced by a process comprising:

providing a parent strain of *Lactococcus* species comprising a thymidylate synthase gene comprising

at least 100 contiguous nucleotides that are at least 90% identical to SEQ ID NO: 1; and

at least 100 contiguous nucleotides that are at least 90% identical to SEQ ID NO:2; and

altering by gene disruption said *Lactococcus* thymidylate synthase gene of the parent strain so as to inactivate the thymidylate synthase encoded thereby, ~~wherein the gene encoding said heterologous prophylactic or therapeutic molecule is integrated within, or replaces a part of or the entire thymidylate synthase gene.~~

33. (Currently amended) The isolated *thyA* mutant of a parent strain of *Lactococcus* species according to claim 32, wherein said *Lactococcus* thymidylate synthase gene comprises a ~~nucleotide sequence selected from the group consisting of~~ SEQ ID NO: 3 ~~[[and]]~~ or SEQ ID NO: 5.

34. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species according to claim 32, wherein ~~altering said *Lactococcus* thymidylate synthase gene to inactivate the *Lactococcus* thymidylate synthase encoded thereby~~ comprises gene disruption the gene encoding the heterologous therapeutic molecule is integrated within, or replaces at least a part of the thymidylate synthase gene.

35. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species according to any of claims 32, 34, 37 or 38, wherein the *Lactococcus* species is *Lactococcus lactis*.

36. (Cancelled).

37. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species according to claim 32, wherein said (*thyA*) mutant is transformed with a transforming plasmid,

wherein said transforming plasmid does not encode an active thymidylate synthase.

38. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species according to claim 37, wherein the transforming plasmid comprises the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule.

39. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species according to any of claims 32, 34, 37, or 38, wherein is the gene encoding a heterologous ~~prophylactic or~~ therapeutic molecule encodes Interleukin-10.

40-41. (Cancelled).

42. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species according to any of claims 32, 34, 37, or 38, wherein the gene encoding a heterologous ~~prophylactic~~ or therapeutic molecule encodes Interleukin-10 and wherein the *Lactococcus* species is *Lactococcus lactis*.

43-64. (Cancelled).

65. (Currently amended) The composition of claim 12, wherein said (*thyA*) mutant is ~~further~~ transformed with a transforming plasmid,
wherein said transforming plasmid does not encode an active thymidylate synthase.

66. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of claim 21, wherein the gene encoding a heterologous ~~prophylactic~~ or therapeutic molecule is integrated within, or replaces a part of or the entire thymidylate synthase gene of said parent strain of *Lactococcus* species.

67. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species, said *thyA* mutant comprising:

lacking an ~~inactive~~ active *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous ~~prophylactic~~ or therapeutic molecule; and

wherein said *thyA* mutant expresses the heterologous therapeutic molecule, and wherein the *thyA* mutant is produced by a process comprising:

providing a parent strain of *Lactococcus* species comprising a *Lactococcus* thymidylate synthase gene; and

altering said *Lactococcus* thymidylate synthase gene to inactivate the thymidylate synthase encoded thereby, wherein the gene encoding said heterologous ~~prophylactic~~ or therapeutic molecule is ~~interpreted~~ integrated within or replaces a part of or the entire thymidylate synthase gene.

68. (Currently amended) The isolated thymidylate synthase (*thyA*) mutant of a parent strain of *Lactococcus* species of any one of claims 1, 2, 5, 6, 12, 13, 21, 22, 24, 25, 30-34, 37, 38, 65, or 66, wherein said parent strain of *Lactococcus* species is MG1363.

69. (New) A *Lactococcus* species of the type that is alive and has a genome, wherein the improvement comprises:

integrating into the genome a nucleotide sequence encoding a molecule heterologous to *Lactococcus*, which molecule is capable of being expressed by the *Lactococcus* species and is further therapeutic in a human, said nucleotide sequence being integrated into the genome so as to at least partially replace a *Lactococcus*' thymidylate synthase gene, said integration rendering said *Lactococcus* species devoid of thymidylate synthase activity, wherein the *Lactococcus* species expresses the molecule after ingestion by the human in the human's gut, but wherein the *Lactococcus* species does not survive outside of the human's gut in the absence of thymine or thymidine.

70. (New) The *Lactococcus* species of claim 69, which is *Lactococcus lactis*.

71. (New) The *Lactococcus* species of claim 69, wherein the nucleotide sequence encodes human Interleukin-10.

72. (New, withdrawn) A method for delivering a heterologous molecule to a human subject, the method comprising administering the *Lactococcus* species of claim 69 to the human subject.